

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
 GlaxoSmithKline Services Unli
 Attn. Giddings, Peter J.
 980 Great West Road
 Brentford
 Middlesex TW8 9GS
 UNITED KINGDOM

GlaxoSmithKline
 Corporate IP
 Received BRENTFORD
 21 JAN 2005

ATTY: ARG/PMW	DMM: PC
IPM: N/A	ON UPLOADED ON: 21/01/05
ATTY CHECKED/FIILED (day/month/year)	

PCT
 GlaxoSmithKline
 Corporate IP
 Received Stevenage
 21 JAN 2005

(PCT Rule 44.1)

21/01/2005

Applicant's or agent's file reference

ARG/PB60476

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/EP2004/009819

International filing date

02/09/2004 GlaxoSmithKline Corporate IP

Applicant

GLAXO GROUP LIMITED

24 JAN 2005

Received Stevenage

1. The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority
 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
 Fax: (+31-70) 340-3016

Authorized officer

Josef Ullrich

BEST AVAILABLE COPY

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/ is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]: "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in canceling some claims and in adding new claims]: "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ARG / PB60476	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT / EP2004 / 009819	International filing date (day/month/year) 02/09/2004	(Earliest) Priority Date (day/month/year) 04/09/2003
Applicant GLAXO GROUP LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. 1.

2. Certain claims were found unsearchable (See Box II).

3. Unity of invention is lacking (see Box III).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

PROCESS FOR THE PREPARATION OF (1S,4R)-CIS-4-(2-AMINO-6-CHLORO-9H-PURIN-9-YL)-2-CYCLOPENTENE-1-METHANOL

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. none of the figures is to be published with the abstract.

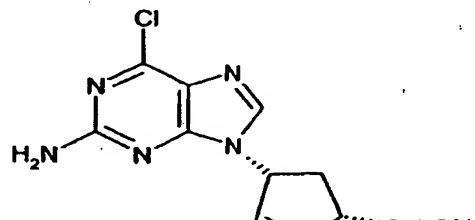
INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/009819

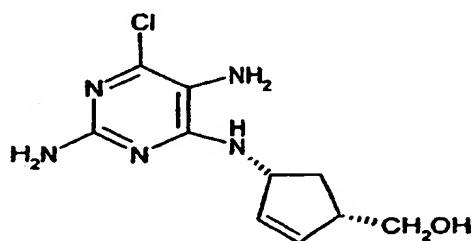
Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

A process for preparing a chloropurine compound of formula (I)



(I)

or a derivative thereof, which comprises ring closure of the compound of formula (VII) or a derivative thereof



(VII)

in the presence of catalytic acid and at least one equivalent of a formate derivative.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/009819

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D473/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/19327 A (ACTIONTEC ELECTRONICS INC) 6 April 2000 (2000-04-06) cited in the application examples A-D -----	1-10
A	EP 0 628 044 A (WELLCOME FOUND) 14 December 1994 (1994-12-14) example 25 -----	1-10
A	EP 0 741 710 A (WELLCOME FOUND) 13 November 1996 (1996-11-13) example 11b ----- -/-	1-10

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

13 December 2004

Date of mailing of the international search report

21/01/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Baston, E

1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/009819

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	VINCE ET AL: "Synthesis and Anti-HIV Activity of Carbocyclic 2',3'-Didehydro-2',3'-dideoxy 2,6-Disubstituted Purine Nucleosides" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 33, no. 1, 1990, pages 17-21, XP002109188 ISSN: 0022-2623 page 20; example 6a -----	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/009819

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 0019327	A 06-04-2000	US AU TW WO	6119162 A 6057599 A 432328 B 0019327 A1	12-09-2000 17-04-2000 01-05-2001 06-04-2000
EP 0628044	A 14-12-1994	AT AU AU AU CA DE DE DK EP ES WO HK JP JP PT US US US US US	245646 T 707075 B2 2489197 A 3571093 A 2130755 A1 69333109 D1 69333109 T2 628044 T3 0628044 A1 2203615 T3 9317020 A2 1003941 A1 3172533 B2 7504185 T 628044 T 2001008946 A1 5641889 A 5840990 A 5919941 A 5808147 A	15-08-2003 01-07-1999 28-08-1997 13-09-1993 26-08-1993 28-08-2003 15-04-2004 17-11-2003 14-12-1994 16-04-2004 02-09-1993 06-02-2004 04-06-2001 11-05-1995 31-12-2003 19-07-2001 24-06-1997 24-11-1998 06-07-1999 15-09-1998
EP 0741710	A 13-11-1996	AT AU AU BR DE DE DK EP FI GR HK HU JP NO NZ PL RU SI US US CA CN CN ES WO IL PT SG TW US US US	192742 T 690203 B2 1543895 A 9506667 A 69516847 D1 69516847 T2 741710 T3 0741710 A1 963070 A 3033850 T3 1004087 A1 75300 A2 9508412 T 963239 A 278948 A 315713 A1 2140913 C1 741710 T1 6448403 B1 5917041 A 2182105 A1 1388123 A 1139924 A ,B 2148486 T3 9521161 A1 112539 A 741710 T 47918 A1 390877 B 2002173649 A1 2003187263 A1 6552193 B1	15-05-2000 23-04-1998 21-08-1995 16-09-1997 15-06-2000 26-10-2000 14-08-2000 13-11-1996 02-08-1996 31-10-2000 27-10-2000 28-05-1997 26-08-1997 02-10-1996 26-01-1998 25-11-1996 10-11-1999 31-08-2000 10-09-2002 29-06-1999 10-08-1995 01-01-2003 08-01-1997 16-10-2000 10-08-1995 31-08-2000 29-09-2000 17-04-1998 21-05-2000 21-11-2002 02-10-2003 22-04-2003

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/009819

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0741710	A	US	6087501 A	11-07-2000
		US	5917042 A	29-06-1999
		US	6555687 B1	29-04-2003
		ZA	9500884 A	05-08-1996

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Applicant's or agent's file reference
see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/EP2004/009819

International filing date (day/month/year)
02.09.2004

Priority date (day/month/year)
04.09.2003

International Patent Classification (IPC) or both national classification and IPC
C07D473/00

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Baston, E

Telephone No. +49 89 2399-8229



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/009819

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. **type of material:**
 a sequence listing
 table(s) related to the sequence listing
 - b. **format of material:**
 in written format
 in computer readable form
 - c. **time of filing/furnishing:**
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. **Additional comments:**

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/009819

Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-10
No: Claims

Inventive step (IS) Yes: Claims 1-10
No: Claims

Industrial applicability (IA) Yes: Claims 1-10
No: Claims

2. Citations and explanations

see separate sheet

To section V

The following documents were cited in the search report and were considered for the examination of the present application:

- D1: WO 00/19327 A (ACTIONTEC ELECTRONICS INC) 6 April 2000 (2000-04-06)
- D2: EP-A-0 628 044 (WELLCOME FOUND) 14 December 1994 (1994-12-14)
- D3: EP-A-0 741 710 (WELLCOME FOUND) 13 November 1996 (1996-11-13)
- D4: VINCE ET AL: "Synthesis and Anti-HIV Activity of Carbocyclic 2',3'-Didehydro-2',3'-dideoxy 2,6-Disubstituted Purine Nucleosides" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 33, no. 1, 1990, pages 17-21, XP002109188 ISSN: 0022-2623

The present application is directed to a ring closure procedure for compound (VII) resulting in the formation of compound (I), which itself is a precursor for the manufacture of the antiviral compound abacavir. The essential feature of the process is the use of a catalytic amount of an acid. All documents of the prior art make use of excess acid (HCl), in order to make process the ring closure. Thus novelty is acknowledged (Art. 33(2) PCT).

From the documents of the prior art a skilled person would not have been able to derive that the use of catalytic amounts of an acid (e.g. H₂SO₄ conc) like in the examples results in the formation of the desired product in high yield and high purity. Thus the involvement of an inventive step is acknowledged (Art. 33(3) PCT).

Claim 10 is not allowable in view of Rule 6.2(a) PCT, since it refers to examples from the description.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.